Organization: SRI International

Title: CEDAR: Modeling and Optimization of Micromachined Porous Structures for Flow-Through Affinity-Based Biosensors

MTO **Simbiosys**

Start Date: July 2001 **End Date:** June 2006

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Project Goals

Short-term: Develop mathematically convex models and optimization algorithms for the design of engineered microstructures used in flow-through affinity-based (FloTAB) biosensors.
Long-term: Develop a library of computationally efficient models and optimization algorithms for the design of affinity-based biosensors in a variety of multiplexed formats.

Technical Approach

- Choose one or more scalable microstructures (e.g., channels, hexagonal array of pillars) and assay formats as initial candidates for fabrication/testing/modeling
- Experimentally characterize these structures (e.g., surface area, flow rates, analyte capture fraction, non-specific binding, transducer signal-to-noise ratio) with respect to engineering design variables (e.g., structure dimensions, surface energy, Ab density, capillary pressure) and fixed parameters (e.g., analyte and reporter diffusion and kinetic rates, microfabrication constraints).
- Develop mathematically convex models of individual physico-chemical properties (e.g., flow rate vs. channel dimensions, capture fraction vs. flow rate, NSB background vs. rinse time)
- Develop convex models of coupled device processes, assay performance, and engineering constraints
- Validate models against measured characteristics; iterate the fabricate/test/model cycle
- Develop computationally efficient design optimization algorithms based on the convex models developed
- Explore FloTAB biosensor design tradeoffs using the models and optimization algorithms developed
- Phase 2: Generalize models and algorithms to design multiplexed sensors in a variety of formats; validate a benchmark design; technology transfer

Recent Accomplishments

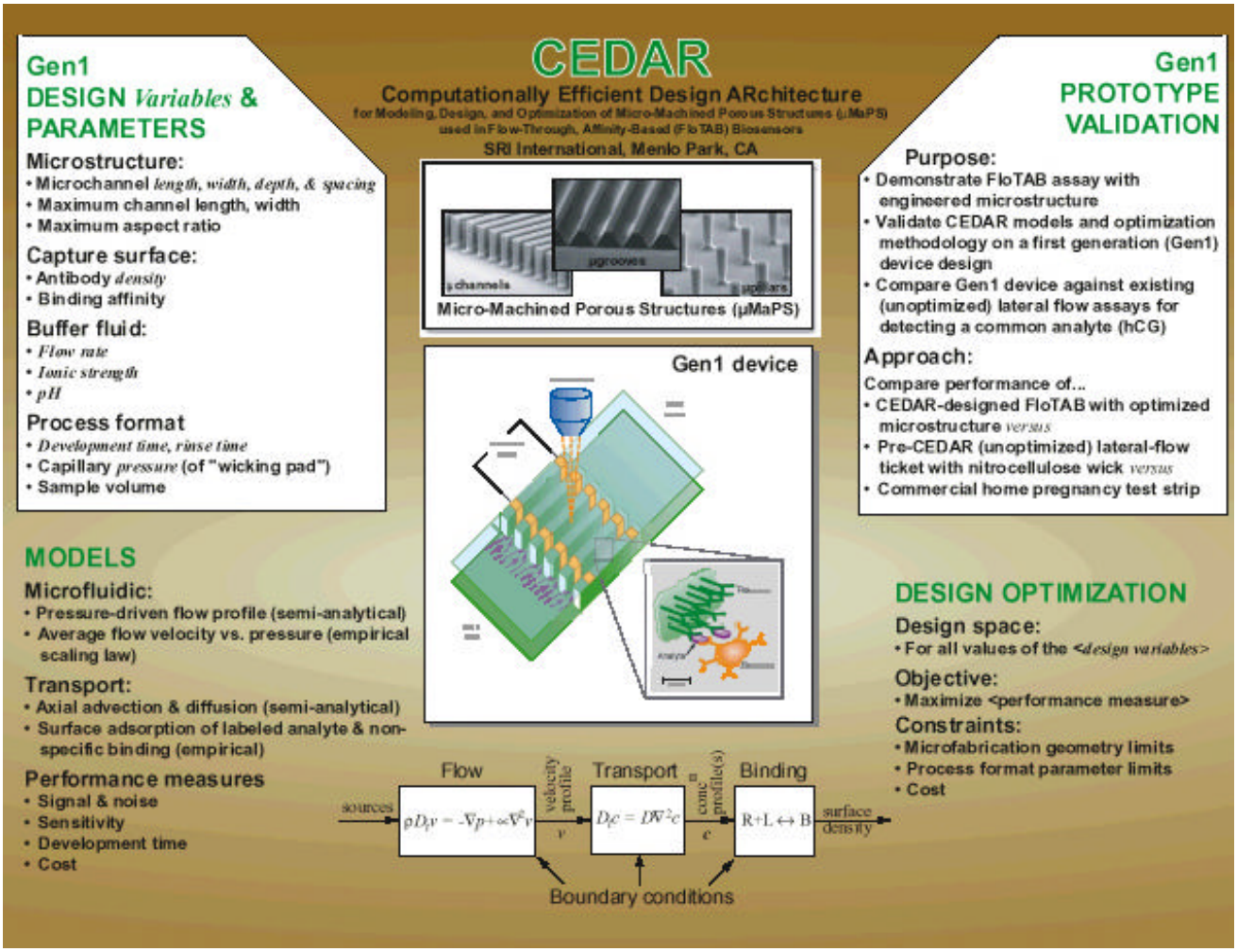
- Identified candidate design variables and parameters for modeling microfluidic flow, analyte diffusion and surface capture, and optical and electrochemical transduction in FloTAB devices.
- Initiated the transformation of these models into mathematically convex form.
- Started the associated experimental effort: microfabricated substrates, surface functionalization chemistry, flow visualization, and binding kinetics.
- Defined a first generation (Gen1) prototype FloTAB assay design problem and a protocol for quantitative comparison of this optimized device with existing (unmodeled and unoptimized) assays.

Six-Month Milestones

- Fabricate and characterize Gen1 device behavior: microfluidic flow, capture fraction, non-specific binding, and optical and electrochemical output signals.
- Construct models of device performance (development time, sensitivity, cost), convex in the design parameters.
- Optimize the Gen1 device design based on these models.
- Fabricate and validate the optimized Gen1 design; compare to unmodeled/unoptimized assays.

Team Member Organizations

N/A


CEDAR
Computationally Efficient Design ARchitecture
for Modeling, Design, and Optimization of Micro-Machined Porous Structures (μMaPS) used in Flow-Through, Affinity-Based (FloTAB) Biosensors
SRI International, Menlo Park, CA
Gen1 DESIGN Variables & PARAMETERS
Microstructure:
• Microchannel length, width, depth, & spacing
• Maximum channel length, width
• Maximum aspect ratio
Capture surface:
• Antibody density
• Binding affinity
Buffer fluid:
• Flow rate
• Ionic strength
• pH
Process format
• Development time, rinse time
• Capillary pressure (of "wicking pad")
• Sample volume
Micro-Machined Porous Structures (μMaPS)
Gen1 device
Gen1 PROTOTYPE VALIDATION
Purpose:
• Demonstrate FloTAB assay with engineered microstructure
• Validate CEDAR models and optimization methodology on a first generation (Gen1) device design
• Compare Gen1 device against existing (unoptimized) lateral flow assays for detecting a common analyte (hCG)
Approach:
Compare performance of...
• CEDAR-designed FloTAB with optimized microstructure versus
• Pre-CEDAR (unoptimized) lateral-flow ticket with nitrocellulose wick versus
• Commercial home pregnancy test strip
MODELS
Microfluidic:
• Pressure-driven flow profile (semi-analytical)
• Average flow velocity vs. pressure (empirical scaling law)
Transport:
• Axial advection & diffusion (semi-analytical)
• Surface adsorption of labeled analyte & non-specific binding (empirical)
Performance measures
• Signal & noise
• Sensitivity
• Development time
• Cost
Flow
Transport
Binding
sources
velocity profile
conc. profile(s)
surface density
Boundary conditions
DESIGN OPTIMIZATION
Design space:
• For all values of the <design variables>
Objective:
• Maximize <performance measure>
Constraints:
• Microfabrication geometry limits
• Process format parameter limits
• Cost